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EXAMINER	
UNGAR, SUSAN NMN	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 01/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/041,030	POWERS ET AL.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *October 21, 24*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *1-7, 8-13 drawn to Pellino 1 assay, 14-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *8-13 drawn to Pellino 2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/22/03, 7/15/02,* 10/21/02
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. The Election filed October 21, 2004 in response to the Office Action of September 20, 2004 is acknowledged and has been entered. Claims 1-37 are pending in the application and Claims 1-7, 8-13 as they are drawn to a method of detecting cancer cells comprising detecting increased copy number of gene encoding Pellino 1, 14-37 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions. Claims 8-13 drawn to a method of detecting cancer cells comprising detecting an increased copy number of a gene encoding Pellino 2, SEQ ID NO:4 are currently under prosecution.

2. Applicant's election with traverse of Group 16, claims 8-13 in Paper submitted October 21, 2004 is acknowledged. The traversal is on the ground(s) that the examination of Groups 7-12 and 16-18 would not constitute an undue burden on the examiner since a proper search would likely encompass both nucleic acid and protein sequences. The argument has been considered but has not been found persuasive as drawn to the rejoinder of claims drawn to detection of cancer comprising detecting overexpression of Pellino 2 polypeptide because Applicant is requesting rejoinder of claims drawn to detection of a different sequence, using materially distinct methods which differ at least in objectives, method steps, reagents and/or dosages and/or schedules used, response variables, and criteria for success. The literature search, particularly relevant in this art, is not coextensive and different searches and issues are involved in the examination of each group. For the reasons set forth above, the restriction requirement is deemed to be proper and is therefore made FINAL.

Further, as drawn to the linking claim restriction drawn to detection of epithelial cancer comprising assaying nucleic acid encoding Pellino 2 polypeptide,

upon review and reconsideration in view of the teaching in the specification as well as Applicant's arguments, Groups 16-18 drawn to epithelial cancers are hereby rejoined.

Specification

3. The specification on page 1 should be amended to reflect the status of the parent application serial number 60/259,502.

4. The disclosure is objected to because it contains embedded hyperlinks, see pages 25 and 35, and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required.

Claim Objections

5. Claims 8-13 are objected to because they recite limitations drawn to non-elected inventions that have been withdrawn from consideration.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:
> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 8-13 are rejected under 35 USC 112, first paragraph, as lacking an adequate written description in the specification.

It is noted that claim 10 is drawn to a method of detecting cancer cells comprising detecting an increased copy number of a gene encoding **an** (emphasis

added) amino acid sequence of SEQ ID NO:4, which clearly reads on a gene encoding a variant of SEQ ID NO:4, a polypeptide comprising am amino acid sequence with at least 70% identity to SEQ ID NO:4. Thus, it is assumed for examination purposes that claim 10 is drawn to detecting an increased copy number of a gene encoding a Pellino 2 polypeptide comprising at least 70% identity with SEQ ID NO:4.

Claims 8-13 are drawn to a method of detecting cancer cells comprising detecting an increase in copy number of a gene encoding a Pellino 2 polypeptide comprising at least 70% identity to SEQ ID NO:4, which reads not only on the identified SEQ ID NO:3 and degenerate variants of SEQ ID NO:3, but also on any gene regardless of degeneracy that encodes a Pellino 2 polypeptide comprising at least 70% identity to SEQ ID NO:4. The findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by

> members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a DNA product itself logically cannot adequately describe a method of using that product.

Thus, the instant specification may provide an adequate written description of a gene encoding a Pellino 2 polypeptide comprising at least 70% identity to SEQ ID NO:4, or degenerate variants of SEQ ID NO:3, with increased copy number that can be used to detect cancer cells, per Lilly by structurally describing a representative number of genes encoding a Pellino 2 polypeptide comprising at least 70% identity to SEQ ID NO:4 or degenerate variants of SEQ ID NO:3 with increased copy number that can be used to detect cancer cells or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe a gene encoding a Pellino 2 polypeptide comprising at least 70% identity to SEQ ID NO:4,or degenerate variants of SEQ ID NO:3, with increased copy number that can be used to detect cancer cells in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of any gene encoding a Pellino 2 polypeptide comprising at least 70% identity to SEQ ID NO:4, or degenerate variants of SEQ ID NO:3, other than SEQ ID NO:3, nor does the

specification provide any partial structure of such genes, nor any physical or chemical characteristics of the genes nor any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification discloses a single gene encoding a Pellino 2 polypeptide comprising at least 70% identity to SEQ ID NO:4 (see Sequence Listing, SEQ ID NO:3), this does not provide a description of the genes encoding a Pellino 2 polypeptide comprising at least 70% identity to SEQ ID NO:4, or degenerate variants of SEQ ID NO:3, with increased copy number that can be used to detect cancer cells that would satisfy the standard set out in Enzo.

The specification also fails to describe a gene encoding a Pellino 2 polypeptide comprising at least 70% identity to SEQ ID NO:4, or degenerate variants of SEQ ID NO:3, with increased copy number that can be used to detect cancer cells by the test set out in Lilly. The specification describes only a single a gene encoding a Pellino 2 polypeptide comprising at least 70% identity to SEQ ID NO:4 with increased copy number that can be used to detect cancer cells. Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the specification does not provide an adequate written description of a gene encoding a Pellino 2 polypeptide comprising at least 70% identity to SEQ ID NO:4, or degenerate variants of SEQ ID NO:3, with increased copy number that can be used to detect cancer cells that is required to practice the claimed invention. Since the specification fails to adequately describe the gene encoding a Pellino 2

polypeptide comprising at least 70% identity to SEQ ID NO:4, or degenerate variants of SEQ ID NO:3, with increased copy number that can be used to detect cancer cells, it also fails to adequately describe the claimed method.

Therefore, only a method of detecting cancer cells in a biological sample from a mammal comprising detecting an increase in copy number of SEQ ID NO:3 but not the full breadth of the claims meets the written description provisions of 35 USC 112, first paragraph.

8. If Applicant were to be able to overcome the rejection under 35 USC 112, first paragraph set forth above, claims 8-10 and 13 would still be rejected under 35 USC 112, first paragraph because while being enabling for a method of detecting epithelial cancer cells in a biological sample from a mammal comprising detecting an increase in copy number of a gene encoding Pellino 2 polypeptide comprising 70% amino acid identity to SEQ ID NO:4 does not reasonably provide enablement for a method of detecting cancer cells in a biological sample from a mammal comprising detecting an increase in copy number of a gene encoding Pellino 2 polypeptide comprising 70% amino acid identity to SEQ ID NO:4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to a method of detecting cancer cells comprising detecting an increase in copy number of a gene encoding Pellino 2 polypeptide comprising 70% amino acid identity to SEQ ID NO:4. This means any type of cancer including cancers that are not epithelial cancers. The specification teaches that in one embodiment, the cancer cells are from an epithelial cell, is an ovarian, colon, or lung cancer (p. 4) and further teaches that epithelial cancers, include

colorectal, lung, breast, prostate, kidney, stomach, bladder, or ovarian cancer, or any cancer of the gastrointestinal tract wherein a preferred embodiment is drawn to lung, colon or ovarian cancer (p. 7) and reiterates this teaching on page 35. Finally, the specification exemplifies increased copy number of SEQ ID NO:3 in tumor samples from lung, colon and ovarian tumors, compared to normal controls (p. 55).

One cannot extrapolate the teaching of the specification to the scope of the claims because it is well known in the art that cancers comprise a broad group of malignant neoplasms divided into two categories, that is carcinomas and sarcomas. Carcinomas are epithelial cancers which originate in epithelial tissues while sarcomas develop from connective tissues and those structures that had their origin in mesodermal tissues (Taber's Cyclopedic Medical Dictionary, F.A. Davis and CO., Philadelphia, 1985, p. 274) wherein the cells are specialized to give rise to the connective tissues, that is bone, cartilage, muscle, the urogenital system and the vascular system (Alberts et al, Molecular Biology of the Cell, Garland Publishing, Inc, NY, 1983, pgs 821-822). Although the specification clearly demonstrates that a subset of epithelial cancer cells in several epithelial cancer types have amplified copy number of SEQ ID NO:3, Osband and Ross (Immunology Today, 1990, 11:193-195) teach that the biochemistry, antigenicity and metastatic potency of neoplastic cells show considerable variation and that there is an obvious heterogeneity of tumors not only between patients but even between metastatic sites within a single patient (p. 194, para 2). Clearly there is heterogeneity between the expression of markers within a single cancer type and even between primary and metastatic cells in the same patient. Thus the finding that copy number of SEQ ID NO:3 is amplified in a subset of several types of epithelial cancers,

allowing detection of cancer cells in several epithelial, cancers is unexpected. However, given the art recognized physical differences between epithelial cells and cells of connective and mesodermal origin, it can not be predicted, nor would it be expected that the same marker, that is the amplification of SEQ ID NO:3 copy number, would also be found in cancer cells that were not of the same lineage as the epithelial cell types. The specification provides insufficient guidance with regard to this issue and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the invention would function as claimed, with any cancer cell type other than epithelial cancer, with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

9. No claims allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at 571-272-0787. The fax phone number for this Art Unit is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 872-9306.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this

application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

Susan Ungar
Primary Patent Examiner
December 29, 2004